children's
MEDICAL CENTER OF DALLAS

December 9, 2003

Center for
Pediatric Gastroenterology

John M Andersen, M D
Medical Director

Carol A Reddel, M D
Norberto Rodriguez-Baez, M D

Michael Russo, M D
Fellow
Eduardo Beltroy, M D
Fellow
Ashish Patel, M D
Fellow

Robin Landgraf, R N , C PN P
Nurse Practitioner

Stephan Moore
Operations Director
Ashleigh Marcus
Program Manager

Affiliated with
Department of Pediatrics
The University of Texas
Southwestern Medical Center
at Dallas

Joe Neely, M D.
8325 Walnut Hill Lane #22
Dallas, Texas 75231
Telephone # 214-691-3535
Fax # 214-691-0404

RE: WILLIAMS, LABREA A.
MR#: 870263
FIN#: 000034170092
DOB: 07/20/1994
DOV: 12/09/2003

Dear Dr Neely

Thank you for allowing us to participate in the care of your patient, Labrea Williams. We were happy to see Labrea at the Pediatric Gastroenterology Clinic at Children's Medical Center of Dallas on December 9, 2003 As you well know, Labrea is a 9-year-old African American female with past medical history significant for Stevens-Johnson syndrome in June of 2002 and history of constipation

Labrea presents to the clinic this afternoon with her father as well as other siblings and states that overall Labrea has been doing great, denies any major problems at this time, has no concerns Labrea denies any complaints or concerns at this time. They deny any recent history of fever, vomiting, or diarrhea. The state that Labrea has been tolerating p.o without difficulty She has been urinating and stooling normally She has been stooling daily with no blood or pain on stool. The discontinued the use of MiraLax, and she continues to stool daily without any difficulty. They have no other concerns at this time

Labrea is currently not on any medications. She currently has Advil listed as her only allergy which was the suspected cause of her Stevens-Johnson syndrome

PHYSICAL EXAMINATION. Today, the patient's temperature was 97.9 degrees Fahrenhert, heart rate 84, respiratory rate 18, blood pressure 114/60, height 142 cm, up from 133 5 cm approximately a year ago Weight is up to 57.7 kg, up from about 46.7 kg, also approximately a year ago.

RE: WILLIAMS, LABREA A.
MR#. 870263
Page 2

On physical exam today, the patient is well developed, well nourished, in no acute distress. Pupils were equal, round, and reactive to light Tympanic membranes were clear bilaterally. Nasopharynx and oropharynx were clear. The neck was supple, no lymphadenopathy Cardiovascularly, regular rate and rhythm, on murmur. Lungs were clear to auscultation bilaterally, no wheezing. Abdomen was soft, nontender, nondistended, positive bowel sounds. Skin has had multiple hypo and hyperpigmented spots noted throughout. Neurologic exam was normal with symmetric reflexes. Psychiatry: the patient was responsive, and mental status was appropriate for age

IMPRESSION: Labrea is a 9-year-old African American female with past medical history significant for Stevens-Johnson syndrome and history of constipation. The patient has no acute issues at this time.

RECOMMENDATIONS: The parents have discontinued the use of MiraLax and state that she is having normal bowel movements at this time. They were instructed that they may resume the MiraLax if constipation symptoms recur They were instructed to use MiraLax 17 grams p.o. q.d. There are no other active gastrointestinal issues at this time, and we have discharged her from the Gastroenterology Clinic to follow up with her primary care pediatrician, yourself. If any negative problems or concerns arise, they may contact our nurse at 214-456-8071, Aurora Bustillos.

If you have any questions or concerns regarding this treatment plan, please do not hesitate to contact us.

[redacted]
DPN

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RE: WILLIAMS, LABREA A.
MR#: 870263
Page 3

The patient will be discharged to your care. If any new problems do arise, we will be happy to see her at any time. You can contact our nurse, Aurora, at the number listed above

Sincerely,

Ashish Patel, M.D.
Pediatric Gastroenterology Fellow

Norberto Rodriguez-Baez, M.D.
Assistant Professor
Pediatric Gastroenterology

	AP / 27
D	12/09/2003
T	12/10/2003
JOB#	-142012

[redacted]
DPN

[redacted]

CHILDREN'S MEDICAL CENTER OF DALLAS
1935 Motor Street • Dallas, Texas 75235 • (214) 456-7000

GASTROENTEROLOGY AND NUTRITION DEPARTMENT
TREATMENT PLAN *(PLAN DE TRATAMIENTO)*

MR # / ID NO: 07/20/1994 Gastro
PATIENT: WILLIAMS, LABREA AU'BRYA
000870263 34170092
DATE: 12/09/2003 RODRIGUEZ-BAEZ, NORBERTO
D T
DOB:

Diagnosis *(Diagnosis)*: Stevens Johnson, Constipation

Radiology *(Radiología)*: ϕ

Procedure *(Procedimiento)*: ϕ

Labs *(Laboratorio)*: ϕ

Medications *(Medicamentos)*: ☒ No change *(Ningún cambio)*
Changes *(Cambios)* Miralax 17grams in 8ounces of fluid everyday

Diet *(Dieta)*: ϕ

Education/Teaching *(Educación/Enseñanza)*: ϕ

Follow-up *(Proxima cita)*:

☐ We would like to see your child in Discharged from clinic Please make an appointment
(Queremos ver a su hijo/a en _____ *Por favor haga una cita)*

☐ To be determined after evaluating test results
(Será determinada después de una evaluación de los resultados)

☒ Call if having problems *(Llame si tiene problemas)* 214 456-8071 Aurora Bustillos RN

☐ Other *(Otra información)* _____

If you have any questions, please contact our office at (214) 456-8000 or (800) 568-8937 Someone will be available 24 hours a day We depend on you playing an active role in your child's care

Si tiene preguntas, por favor llame a nuestra oficina al (214) 456-8000 o (800) 568-8937 Alguien estará disponible 24 horas al dia Dependemos de su participacion en el cuidado de su hijo/a

Discharge instructions reviewed with and copy given to parents

[redacted] 12/9/3 16:20 Aurora Bustillos RN 12/9/3 16:28
Signature/Title Date/Time Signature/Title Date/Time

CMC62500-012NS (03/03) Original - Medical Records Yellow - Department Copy

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[redacted]
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PCP Nealy (Letts)

07/20/1994 Gastro
WILLIAMS, LABREA AU'BRYA
000870263 34170092
RODRIGUEZ-BAEZ, NORBERTO
12/09/2003 D T

9yrs

CHILDREN'S MEDICAL CENTER OF DALLAS
1935 Motor Street • Dallas, Texas 75235 • (214) 456-7000

Center for Pediatric Gastroenterology and Nutrition
OUTPATIENT FOLLOW-UP VISIT FORM

Sources of Information

Informant Signature LaBrea Williams Relationship to Patient Stepfather

Chief Complaint

Problem being followed Steven Johnson Is it under control? ☒ Yes ☐ No

Concerns today check-up ∅ complaints / problems ∅ F/V/D
eating well stool daily ∅ blood/pain stopped Miralax

Hospitalizations, emergency visits, operations since last office visit NO

Current medications (list name, dose, frequency) NONE

Past History

Immunizations ☒ Up to date ☐ Missing

Allergies ☐ None ☒ Yes If yes, please list medication and reaction ADVIL

First menses ______ ☒ N/A Regular periods? ☐ No ☐ Yes Last menstrual period ______

Does your child have any chronic medical problems? ☒ No ☐ Yes

If yes, please list ______

Family History

Are there any chronic medical problems in the family? ☒ No ☐ Yes

If yes, please list ______

Social History

Primary caretaker ______ Child in daycare? ☒ No ☐ Yes

Are there any new stresses at home? ☒ No ☐ Yes If yes, please list ______

Review of Systems

Does your child have troubles with any of the following areas? Check all that apply

☐ Brain ☒ Eyes (glasses) ☐ Nose ☐ Lungs ☐ Kidneys ☐ Blood ☐ Joints
☐ Bones ☐ Ears ☐ Mouth ☐ Heart ☐ Skin ☐ Immune system

Physical Examination

BELOW THIS LINE FOR OFFICE USE ONLY CFlores WA

Vital Signs Temp 97.9 (O) HR 84 RR 18 Ht 142 (75%) Wt 57.7 (95%)
BP 114-60 FOC ____ (%) Pain 0 ☒ VAS ☐ FACES ☐ FLACC Last Ht 133.5 (11) Last wt 46.7 (11)

		NE	Yes	No	
General	Well developed and nourished, no distress	☐	☒	☐	
Eyes	PERRL, conjunctivae clear	☐	☒	☐	
Ears	External ears and tympanic membranes normal	☐	☒	☐	
Nose	External nose and nasal mucosa normal	☐	☒	☐	
Mouth	Lips, teeth and mouth normal in appearance	☐	☒	☐	
Neck	Supple, no abnormal adenopathy, trachea midline	☐	☒	☐	
Chest	Respirations comfortable, chest clear	☐	☒	☐	
Heart	Regular rate and rhythm, femoral pulses 2+ and equal	☐	☒	☐	
Abdomen	Soft, nondistended, nontender, without organomegaly or mass	☐	☒	☐	
Rectal	Normal, stool guaiac negative	☒	☐	☐	
Genitalia	Normal development (Tanner I II III IV V)	☒	☐	☐	
Skin	Clear of significant visible or palpable lesions	☐	☐	☒	multiple hyper/hypo pigmented spots
Lymphatic	No inguinal or cervical adenopathy	☒	☐	☐	
Neurologic	Alert, tone normal, knee jerk DTR's 1-3, symmetric	☒	☐	☐	
Psych	Responsive, mental status normal for age	☒	☐	☐	

MD Notes Assessment

Imp/ ① Stevens Johnson
② Constipation

Recs/ 1- continue miralax 17 gm qd

Discharged from clinic

Signature

I have reviewed the records, taken the history, examined the patient, and discussed the management plan

[signature] 12/9/3 16:20 [signature] Rodriguez-Baez MD 12-09-03 16:20

Signature/Title Date/Time Signature/Title Date/Time

CMC62503-002NS (08/02)

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APPENDIX 5

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF TEXAS
DALLAS DIVISION

LASANDRA MADDEN, Individually and on Behalf of LABREA WILLIAMS, a minor child,	§	
Plaintiff,	§	
vs.	§	CIVIL ACTION NO. 3:03CV 0167BD
WYETH d/b/a WYETH, INC., f/k/a AMERICAN HOME PRODUCTS CORPORATION; WYETH CONSUMER HEALTHCARE, an unincorporated Division of WYETH, f/k/a WHITEHALL-ROBINS HEALTHCARE; AND WHITEHALL LABORATORIES, INC.,	§	
Defendants.	§	

DECLARATION OF WILLIAM WARDELL, MD, PhD

My name is William Wardell. I am of sound mind and do not suffer from any disability that would prevent me from giving this my affidavit. I have never been convicted of a felony or a crime involving moral turpitude. The information contained herein, to the extent it discusses the joint meeting of the Arthritis Drugs and the Nonprescription Drug Advisory Committees, is within my personal knowledge in that it has been derived from my review of the relevant hearing transcript and is true and correct. The information contained herein, to the extent it discusses Dr. Tackett's report, is within my personal knowledge and is true and correct based upon my review of Dr. Tackett's expert report in this case. The remaining information contained herein is within my personal knowledge and is true and correct and based upon my knowledge, training and experience.

1. I am a licensed physician, and I also have a PhD in Pharmacology, from the University of Oxford. I am Board Certified by the American Board of Clinical Pharmacology.

2. I spent 15 years in Academic Medicine and Clinical Pharmacology, most of it at the University of Rochester Medical Center in Rochester, NY, where I served a Fellowship in Clinical Pharmacology and Medicine, and then went on to a faculty appointment as Associate Professor of Pharmacology and Toxicology, Assistant Professor of Medicine, and Associate Physician at the University's main teaching hospital, Strong Memorial.

3. At the University of Rochester, in addition to teaching medical and graduate students in Pharmacology and Clinical Pharmacology, I was a co-founder of the Clinical Pharmacology consultation service at the University's Strong Memorial Hospital and related hospitals. In that service my responsibilities included diagnosing, evaluating, and helping to manage Adverse Drug Reactions (ADRs), actual or suspected, of all types. I also co-founded the University's Center for the Study of Drug Development (now at Tufts University).

4. After a career in Academic Medicine, I spent the next 20 years in Pharmaceutical Medicine, mostly in the Medical Director role, managing the medical and regulatory functions of Drug Development and also the oversight (especially for safety) of drugs on the market. These responsibilities included Clinical Research, Safety, Regulatory, Protocols, Data Acquisition, Data Management, and Statistics. My responsibilities have included managing Clinical Research on drug efficacy and toxicity, including Adverse Drug Reactions; Regulatory aspects of Drug Development, FDA Approval, and use; and the Safety of marketed drugs, including safety reporting to the FDA. I have had the medical responsibility for both OTC drugs and prescription drugs.

5. With regard to the case of LaBrea Williams, Plaintiffs' expert Dr. Randall Tackett has opined in his report that "a safer alternative design for racemic ibuprofen is enantiomerically pure S-ibuprofen."

6. S-ibuprofen, which is also known as S(+)-ibuprofen, and also as dexibuprofen, has been marketed and sold in Europe for some years. I shall use the name dexibuprofen in the remainder of this document, because that is the approved name. (Racemic ibuprofen, which is the form already available in the US, contains a mixture of R(-)-ibuprofen and dexibuprofen.)

7. Dexibuprofen was evaluated by the US FDA and discussed in public at a joint Committee meeting of the FDA's Nonprescription Drugs Advisory Committee and the Arthritis Drugs Advisory Committee on October 9th, 1996. That joint Committee meeting considered the clinical sections of an NDA submitted by Bayer Corporation, seeking dexibuprofen's approval as an over-the-counter (OTC) drug in the US. The transcript of this joint meeting reflects that, at the end of the meeting, the Committee voted that dexibuprofen should not be approved for OTC use.

8. In its discussion, the joint Committee members felt that there was not enough safety data (in particular, chronic safety data) to prove safety, and not enough information about the optimal dose to be used, to allow dexibuprofen to be marketed at that time in the United States. There was concern that the proposed dose was too high for OTC use. Some members recommended that Bayer should first seek NDA approval for dexibuprofen as a prescription drug, so that its safety profile and appropriate dosage information could be further established during prescription usage, before applying for a switch to OTC use.

9. To date, dexibuprofen has not been approved for either prescription use or for OTC use in the United States.

10. With respect to the European experience relating to dexibuprofen and the medical conditions known as Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (SJS/TEN), it

is my opinion that there is not yet enough information to determine whether dexibuprofen might have a better safety profile for SJS/TEN than the present racemic ibuprofen, because I have reviewed European dexibuprofen labeling and find that it contains SJS/TEN listed under Side Effects.

11. To determine whether dexibuprofen might have a clinically meaningful safety improvement over racemic ibuprofen, with respect to SJS/TEN adverse events, would take considerable time and resources. A controlled study would need at least several million patients to detect a significant difference in such low-frequency events, and the results would not be available for some years to come.

I declare under penalty of perjury that the foregoing is true and correct.

Executed on April 15, 2005

William Wardell

William Wardell, MD PhD